REMARKS

Claims 1-33 are pending in the application. No new matter has been added by way of amendment. As requested by the Examiner, Applicants are submitting herewith copies of an alignment of claimed nucleotide sequences (SEQ ID NO:10 vs. SEQ ID NO:2) showing 40% identity between the sequences and copies of an alignment of polypeptides encoded by claimed nucleotide sequences (SEQ ID NO:3 vs. SEQ ID NO:8) showing 27% identity between the sequences. Reexamination and reconsideration of the claims are respectfully requested.

The Invention

The invention relates to compositions and methods for detoxification or degradation of fumonisin or AP1. The enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained by degradation with other enzymes, such as, for example, previously-described carboxylesterase and amine oxidase enzymes.

The Rejection of Claims Under 35 U.S.C.§112, First Paragraph, Should Be Withdrawn

Enablement

The Office Action (2/11/03, page 2, #2) has maintained the rejection of claims 1-20 and rejected new claims 21-33 under 35 U.S.C. §112, first paragraph, because the specification "does not reasonably provide enablement for a method that employs nucleotide sequences having at least 70%, 80%, or 90% sequence identity to NO: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30 or 32 and 90% or 95% sequence identity to SEQ ID NO: 2, 4, 7, or 10...." This rejection is respectfully traversed. Applicants believe that none of the claims considered by the Examiner specified 70% identity, as indicated by the copy of pending claims submitted in this response. In the event that these claims are not the same as those currently on record with the Examiner, Applicants request that they be notified immediately so that the claims can be corrected appropriately.

The Office Action (pp. 2-3) asserts that "Applicant's arguments...have been fully considered but are not deemed persuasive" and repeats the rejection for the same reasons as

those in the previous Office Action. In maintaining these grounds for rejection, the Office Action is disregarding not only Applicant's arguments but also the case law and guidelines cited in those arguments. Applicants respectfully traverse this rejection and submit that the Office Action is applying an extraordinarily high standard of enablement to the present claims, a standard that is not properly based on case law or on the statute.

Applicants also submit that the Office Action has not met its burden to set forth a reasonable explanation as to why it believes that the scope of the claims is not enabled by the specification. *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993). The Office Action of 2/11/03 "maintains that the scope of the claims is broader than the enabling disclosure for the reasons set forth in the last Office [A]ction." The previous Office Action of 8/27/02 (page 5) states that

> The state of the prior art teaches that sequence identity does not necessarily mean similar function. For example, Lazar *et al.* ... teach a mutation of aspartic acid 47 and leucine 48 of a transforming growth factor alpha results in different biological activities (Title). Broun *et al.* ... teaches as few as four amino acid substitutions can change an oleate 12-desaturase activity to a hydroxylase (Abstract). Applicants should note that the nucleic acids encoding Lazar's and Broun's proteins (mutated and original) would have more than 70% and 80% sequence identity and would hybridize to each other under any stringent conditions. Therefore, it is unpredictable whether any nucleotide sequence that shares 70% or 80% sequence identity to the disclosed sequence or that hybridizes thereto under stringent conditions would encode a protein having detoxification/ degrading fumonisin activity in transgenic plants, especially when coexpressed with other enzymes.

Applicants submit that this reasoning misses the point. The test for enablement in this case is not whether any mutation can result in a change in enzymatic function. Clearly, mutations exist which result in a change in enzymatic function, and one of skill in the art would not be surprised to learn that mutations which changed enzymatic function were mutations of conserved amino acid residues, as reported by Lazar and by Broun. Rather, the test for enablement is whether those of skill in the art would readily be able to make and use the claimed invention, and as discussed further below, those of skill in the art would readily be able to make and use the claimed embodiments. The citation by the Office Action of instances where

mutations change the function of a particular enzyme is **not** a "reasonable explanation as to why it believes that the scope of protection provided by that claims is not adequately enabled by the description of the invention provided in the specification..." *In re Wright*, 999 F.2d at 1561, 27 USPQ2d at 1513. Accordingly, the PTO has not met its burden and the burden has not shifted to the applicant to provide proof that the specification is indeed enabling. *Id.*

Applicants maintain that the claims meet the enablement requirement of 35 U.S.C. §112, first paragraph. The invention relates to compositions and methods for detoxification or degradation of fumonisin or AP1. The enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained by degradation with other enzymes, such as, for example, previously-described carboxylesterase and amine oxidase enzymes. Thus, the claims are drawn to methods and compositions involving a primary nucleotide sequence which encodes a polypeptide having fumonisin esterase activity or amine oxidase activity and a secondary nucleotide sequence which encodes a polypeptide having fumonisin detoxification activity.

In the previous Response (Response of November 27, 2002), Applicants discussed that the claims are enabled by the disclosure. Applicants discussed that those of skill in the art, provided the guidance in the present specification, could readily make and use the invention. It is commonly known that those of skill in the art can readily determine the nucleic acid sequence of a nucleic acid molecule as well as the percent identity between sequences. Assays and procedures are known in the art and provided in the specification by which those of skill in the art may readily determine whether a nucleotide sequence encodes a protein having the specified enzymatic activity or results in the reduction of pathenogenicity of a fungus that produces fumonisin (see, *e.g.*, page 10 and working Examples 3 and 4).

As noted in the specification, particularly for example on pages 9 and 11, the primary nucleotide sequences have been previously disclosed and are known in the art. The enzymes and nucleotide sequences of the present invention provide a means for continued catabolism of the fumonisin-degradation products obtained after degradation with other enzymes, such as, for example, the carboxylesterase and amine oxidase enzymes described in U.S. Patent Nos. 5,716,820, 6,025,188, and 6,229,071. As also discussed, for example, on page 9 of the

specification, the enzyme and nucleotide sequences of the present invention may also be used in combination with amino polyolamine oxidase enzymes. Thus, the primary nucleotide sequence of claim 1 may be a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity, and dependent claims 2 and 3 specify that the primary nucleotide sequence is ESP1 or BEST1, or an amino polyolamine oxidase (APAO), respectively. ESP1 and BEST1 are specific examples of fumonisin esterase enzymes, by which is meant any enzyme capable of hydrolysis of the ester linkage in fumonisin, as discussed on page 11 of the specification. The exemplary ESP1 nucleotide sequence is set forth in SEQ ID NO:12 and the exemplary BEST1 nucleotide sequence is set forth in SEQ ID NO:14.

Thus, one contribution of the present invention is the combined use of these previously-known primary nucleotide sequences and their encoded polypeptides with the novel nucleotide sequences and their encoded polypeptides as provided in the present specification. For this reason, the primary nucleotide sequences are functionally described in independent claims 1, 10, and 18. The primary nucleotide sequences are limited in dependent claims 31 and 33 as having at least 90% sequence identity to the sequence set forth in SEQ ID NO: 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, or 32, and are limited in amended dependent claims 30 and 32 as having at least 95% sequence identity to those exemplary sequences.

Assays for the claimed enzyme activities of the primary nucleotide sequences are known in the art and are also taught in the present specification. Isolation and identification of esterase and amino polyolamine oxidase enzymes from an exemplary organism (*Exophiala spinifera)* are taught by the specification, particularly in working Example 1. Other additional methods are known in the art and taught in patents and applications incorporated by reference into the present specification, for example, U.S. Patent No. 5,716,820, which in Example 2 (column 19) teaches methods of cloning genes that encode fumonisin esterase. U.S. Patent No. 6,025,188, incorporated by reference, teaches in Example 13 a detailed assay for the demonstration of functional esterase activity. The primary nucleotide sequences may be isolated from other organisms, as illustrated by working examples in U.S. Pat. No. 6,211,434 of sequences derived from *Rhinocladiella atrovirens*. These sequences have been incorporated into the sequence listing of the present application as SEQ ID NOs: 28-33.

In contrast to the primary nucleotide sequences, the secondary nucleotide sequences and their encoded polypeptides were not known in the art prior to the present invention. These sequences are exemplified by the novel sequences disclosed in the present specification. Independent claims 1, 10, and 18 recite that said secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10. Independent claims 19 and 20 recite that said secondary nucleotide sequence comprises at least one sequence selected from the group consisting of a nucleotide sequence set forth in one of SEQ ID NO: 2, 4, 7, and 10. Independent claims 1, 10, and 18 (and therefore dependent claims 2-9, 11-17, and 21-33) also require that the secondary nucleotide sequence encodes a polypeptide having fumonisin detoxification activity. The specification provides guidance for determining percent identity of sequences on pages 17-20 and also teaches assays for fumonisin detoxification or degrading activity, for example, on page 10 and illustrated in working Examples 3 and 4. In this manner, the specification teaches all the limitations of the claimed secondary nucleotide sequences so that one of skill in the art would be able to make and use the invention.

Based on the guidance provided by the specification regarding the claimed nucleotide sequences, the skilled artisan could choose among possible modifications to produce polypeptides within the parameters set forth in the claims and then test these modified variants to determine whether they retain the desired activity.

In the previous Response, Applicants discussed the appropriate standard for determining whether undue experimentation would be required to make and use an invention, including *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). The Federal Circuit has repeatedly stated that enablement is not precluded by the necessity for some experimentation, so long as the experimentation needed to practice the invention is not undue. *Id.* Furthermore, a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance by which the experimentation should proceed. *Id.*

Applicants stress that when evaluating the quantity of experimentation required, the court looks to the amount of experimentation required to practice a single embodiment of the invention, rather than the amount required to practice every embodiment of the invention. For example, in *Wands*, the claims at issue were drawn to immunoassay methods using any

monoclonal antibody having a binding affinity for HbsAg of at least 10^{-9} M. The PTO had taken the position that the claim was not enabled as it would take undue experimentation to make the monoclonal antibodies required for the assay. The Federal Circuit reversed and held that the claims were enabled, as the amount of experimentation required to isolate monoclonal antibodies and screen for those having the correct affinity was not undue. *See Id.* Clearly, the Federal Circuit did not contemplate that every antibody useful in the methods of the claim must be identified. Rather, the court considered the amount of experimentation required to identify one or a few monoclonal antibodies having the required affinity. *See also, Johns Hopkins University v. Cellpro*, 931 F. Supp. 303, 324 (D. Del. 1996), *aff'd in part, vacated in part, and remanded*, 151 F.3d 1342, 47 USPQ2d 1705 (Fed. Cir. 1998) (stating that the "specification need only enable one mode of making the claimed invention.").

A similar conclusion was reached in *In re Jackson*, 217 USPQ 804, 807 (Bd. Pat. App. & Int. 1982). In *In re Jackson*, the Board held that a considerable amount of experimentation is permitted to practice the invention and is not undue if it is merely routine in the art or if the specification provides a reasonable amount of guidance and direction to perform such experimentation. Applicants note that it is now customary in the art to make a number of sequences and assay them for a desired function in order to achieve the best results. For example, such techniques can involve what is commonly referred to as "shuffling," as described for example in U.S. Patent No. 5,837,458, issued November 17, 1998 with inventors Minshull and Stemmer and entitled, "Methods and Compositions for Metabolic and Cellular Engineering."

In such techniques, it is common to mutagenize individual sequences or a set of sequences which are then assayed for a desired activity. In fact, such techniques may even make use of a library of sequences which is recursively mutagenized, screened for function using a functional assay, and re-mutagenized. Examples of the use of such techniques include: Minshull and Stemmer (1999) *Current Opinion in Chemical Biology* 3:284-290, entitled "Protein Evolution by Molecular Breeding"; and Christians *et al.* (1999) *Nature Biotechnology* 17: 259-264, entitled "Directed evolution of thymidine kinase for AZT phosphorylation using DNA family shuffling." Such experiments are designed and are intended to encompass the generation and testing of a very large number of variant sequences for a desired function. As indicated by

these and other publications, this level of experimentation is now considered routine in the art and thus would not be considered "undue experimentation" under *In re Wands* and *In re Jackson*.

The Office Action states on page 4 that

> Absent any clear and convincing evidence as to why all nucleotide sequences having at least 70%, 80%, or 90% sequence identity to [the specified SEQ ID NOs]...are expected to encode a polypeptide having fumonisin detoxification activity, the rejection may be maintained.

The Office Action does not cite any support for this "clear and convincing" standard, and Applicants are aware of none. Thus, it appears that the Office Action, in addition to ignoring the state of the art, has applied an extraordinarily high burden of proof which is not properly applicable to the present situation. Applicants request clarification of the basis for the application of this high burden. Whether or not any such basis exists, Applicants reiterate that the claims are fully enabled.

Applicants further note that the presence of inoperative embodiments does not render the claims invalid. *See, Atlas Powder Co. v. E. I. Du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984) (noting that one of skill in the art would be able to determine which embodiments were operative). Even in an unpredictable art, enablement does not require "disclosure of a test of every species covered by a claim." *In re Angstadt*, 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976) (noting that such a requirement would "force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments" and "would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed.")

In the instant case, the quantity of experimentation required to practice the invention amounts to the steps of stably integrating into a plant or plant cell a primary nucleotide sequence having fumonisin esterase activity or amine oxidase activity and stably integrating into a plant or plant cell a secondary nucleotide sequence that meets the sequence limitation of the claims and that has fumonisin detoxification activity. The transformed plant or plant cell may then be assayed for enzymatic activity and/or increased resistance to fungus. Assays for such enzymatic

activity, while routine in the art, have further been presented in the specification on page 10 and in working Examples 1, 3, and 4.

Ample guidance is therefore provided to allow one of skill in the art to identify additional sequences encompassed by independent claims 1, 10, 18, 19, and 20 (and thus claims 2-9, 21-22, and 29-33, which are dependent on or incorporate the limitations of claim 1; claims 11-17 and 23-25, which are dependent on or incorporate the limitations of claim 10; and claims 26-28, which are dependent on claim 18). Consequently, Applicants submit that the quantity of experimentation necessary to practice the claimed invention is not undue and that the amount of guidance presented in the specification is sufficient to enable the claimed plants, plant cells, and methods of use. Applicants respectfully submit that the rejection of the claims under 35 U.S.C. §112, first paragraph, for lack of enablement should be withdrawn.

Written Description

The Office Action (2/11/03, page 5) has maintained the rejection of claims 1-20 and rejected new claims 21-33 under 35 U.S.C. §112, first paragraph, "as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." The Office Action (page 5) asserts that "Applicants' arguments...have been fully considered but are not deemed persuasive."

In maintaining these grounds for rejection, the Office Action disregards not only Applicants' arguments but also the case law cited in those arguments. Applicants respectfully submit that the Office Action has applied an extraordinarily high standard of written description to the present claims, a standard that is not properly based on case law or on the statute. In addition, Applicants believe that the Office Action has not satisfied the burden of presenting a *prima facie* case of unpatentability by providing evidence or reasons why those of skill in the art "would not recognize in the disclosure a description of the invention." *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1583 (Fed. Cir. 1996). The rejection of the claims as failing to meet the written description requirement is respectfully traversed. This rejection is addressed first with

regard to the secondary nucleotide sequences of the claims and second with regard to the primary nucleotide sequences of the claims.

Independent claims 1, 10, and 18 (and thus claims 2-9, 21-22, and 29-33, which are dependent on or incorporate the limitations of claim 1; claims 11-17 and 23-25, which are dependent on or incorporate the limitations of claim 10; and claims 26-28, which are dependent on claim 18) recite that said secondary nucleotide sequence has at least 90% identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10. Independent claims 1, 10, and 18 also require that the secondary nucleotide sequence encodes a polypeptide having fumonisin detoxification activity. Independent claims 19 and 20 recite that said secondary nucleotide sequence comprises at least one sequence selected from the group consisting of a nucleotide sequence set forth in one of SEQ ID NO: 2, 4, 7, and 10. Claims 21, 23, and 26 recite that the secondary nucleotide sequence has at least 95% sequence identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10, and claims 22, 24, 25, and 28 recite that the secondary nucleotide sequence is the sequence set forth in SEQ ID NO: 2, 4, 7, or 10. Claim 27 recites that the secondary nucleotide sequence encodes the polypeptide set forth in SEQ ID NO: 3, 5, 8, or 11. The specification provides guidance for determining percent identity of sequences on pages 17-20 and also teaches assays for fumonisin detoxification or degrading activity, for example, on page 10 and illustrated in working Examples 3 and 4. In this manner, the specification teaches all the limitations of the claimed secondary nucleotide sequences so that one of skill in the art would appreciate that Applicants were in possession of the claimed invention.

Applicants reiterate that the recitation of at least 90% or 95% sequence identity is a *very predictable structure* of the nucleotide sequences encompassed by the claimed invention. Applicants note that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001). Applicants submit that the knowledge and level of skill in the art would allow a

person of ordinary skill to envision the secondary nucleotide sequences of the claimed invention, *i.e.*, a nucleotide sequence having at least 90% or 95% sequence identity to the sequence set forth in SEQ ID NO: 2, 4, 7, or 10.

Furthermore, the description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See, Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs defined by nucleotide sequence and falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See, Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, First Paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001). The recitation of a predictable structure of at least 90% or 95% sequence identity to SEQ ID NO: 2, 4, 7, or 10 is sufficient to satisfy the written description requirement for the secondary nucleotide sequence of the claims.

Applicants previously cited for support Example 14 of the Revised Interim Written Description Guidelines. The Office Action (page 6) states that the situation described in Example 14 is "not analogous" to the present claims "because the sequence identity of the instant application is based on a nucleotide sequence." Applicants maintain that Example 14 is essentially analogous to the present claims and that the rationale of Example 14 supports Applicants' assertions that the present claims meet the written description requirement. The claims of the present invention encompass secondary nucleotide sequences having at least 90% or 95% sequence identity to SEQ ID NOs: 2, 4, 7, or 10 wherein the polypeptide has fumonisin detoxification activity. As in Example 14, the present specification discloses the nucleic acid sequence of SEQ ID NOs: 2, 4, 7, and 10 and the claims recite a limitation requiring the compound to have a specific function (*i.e.*, fumonisin detoxification or degradative activity). Consequently, contrary to the Examiner's conclusion, the sequences encompassed by the claims are defined by relevant identifying physical and chemical properties. In fact, the common attributes possessed by the members of the secondary nucleotide sequence genus is that they encode

polypeptides having fumonisin degradative or detoxification activity and share at least 90% sequence identity at the nucleotide level to the disclosed nucleotide sequences of SEQ ID NO: 2, 4, 7, or 10. The necessary common features of the claimed genus are clear. Accordingly, the written description requirement has been met.

The Broun *et al.* reference cited by the Examiner (*Science* 282: 1315-1317 (1998)) involved an experiment to determine the function of seven amino acid residues that were strictly conserved between a group of hydroxylase enzymes from *L. fendleri* and *R. communis* and a group of oleate desaturases from *Arabidopsis*, *Z. mays*, *G. max*, *R. communis*, and *B. napus*. The authors exchanged the seven strictly conserved residues between two sets of enzymes: the *Lesquerella* hydroxylase and the desaturases as well as the *Arabidopsis* FAD2 oleate desaturase and the *Lesquerella* hydroxylase. The authors found that exchanging these strictly conserved residues between the enzymes conferred some of the properties of the enzyme which normally contains those conserved residues. In performing this study, the authors performed the following: 1) compared amino acid sequences of multiple enzymes from a collection of plant species; 2) identified highly conserved residues among these sequences; 3) designed novel amino acid sequences to test their hypothesis that the highly conserved residues played an important role in enzymatic activity of the different enzymes; 4) constructed modified nucleotide sequences encoding their designed amino acid sequences; 5) producing stably transformed transgenic plants containing the modified nucleotide sequences; 6) screening those stably transformed transgenic plants for the enzymatic activities of the different enzymes; 7) analyzing the enzymatic activity produced by the transgenic plants. Applicants note that **these steps are *more complicated* than those one of skill in the art would use to practice the presently claimed invention, and yet the Office Action maintains that the present claims are not enabled and do not meet the written description requirement.** Applicants believe that the Broun reference is irrefutable proof that one of skill in the art would be readily able to practice the claimed invention and that therefore the claims meet the enablement and written description requirements of 35 U.S.C. §112.

The claims also discuss limitations relating to primary nucleotide sequences. As discussed in the specification, particularly for example on pages 9 and 11, the novel enzymes and

nucleotide sequences of the present invention provide a means for additional catabolism of the fumonisin-degradation products obtained from degradation with other previously known enzymes, such as, for example, the carboxylesterase and amine oxidase enzymes described in U.S. Patent Nos. 5,716,820, 6,025,188, and 6,229,071. The novel (*i.e.*, "secondary") enzyme and nucleotide sequences of the present invention may also be used in combination with amino polyolamine oxidase enzymes, as also discussed, for example, on page 11. Other amine oxidase enzymes are known in the art. See, for example, U.S. Pat. No. 5,792,931, issued August 11, 1998. Thus, the primary nucleotide sequence of claim 1 may be a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity, and dependent claims 2 and 3 specify that the primary nucleotide sequence is ESP1 or BEST1, or an amino polyolamine oxidase (APAO), respectively. ESP1 and BEST1 are specific examples of fumonisin esterase enzymes, by which is meant any enzyme capable of hydrolysis of the ester linkage in fumonisin, as discussed on page 9 of the specification.

With regard to the primary nucleotide sequences of the claims, independent claims 1, 10, and 18 include the limitation that the primary nucleotide sequence encodes a polypeptide having fumonisin esterase activity or a polypeptide having amine oxidase activity. Applicants have provided exemplary sequences of the primary nucleotide sequences of the claims, for example, as incorporated by reference in the specification on pages 9 and 11 regarding ESP1, BEST1, and animo polyolamine oxidase enzymes. Exemplary sequences of these enzymes and nucleotide sequences encoding them are also included in the sequence listing. Applicants submit that one of skill, using the guidance of the specification, would be able to identify, isolate, and use a primary nucleotide sequence meeting the limitations of the claims, *i.e.*, a polypeptide having fumonisin esterase activity or amine oxidase activity, as exemplified by the referenced sequences. Guidance is provided in the specification, particularly on page 10 and in working Examples 3 and 4.

Assays for the claimed enzyme activities of the primary nucleotide sequence are known in the art and are also taught in the present specification. Isolation and identification of esterase and amino polyolamine oxidase enzymes from an exemplary organism (*Exophiala spinifera)* are taught by the specification, particularly in working Example 1. Other relevant methods to the

practice of the claimed invention are known in the art and taught in the patents and applications incorporated by reference into the present specification. For example, U.S. Patent No. 5,716,820 teaches in Example 2 (column 19) methods of cloning genes that encode fumonisin esterase, and U.S. Patent No. 6,025,188 teaches in Example 13 a detailed assay for the demonstration of functional esterase activity.

While the above guidance is provided in the specification, Applicants emphasize that the primary nucleotide sequence may encode any enzyme having fumonisin esterase activity or amine oxidase activity. The presently claimed invention is drawn to the use of the novel secondary nucleotide sequences in conjunction with enzymes having fumonisin esterase activity or amine oxidase activity such as those previously described and cited in the specification. For these reasons, Applicants believe that the description of the primary nucleotide sequences meets the written description requirement.

Claims 30 and 32 have been amended to specify that the primary nucleotide sequences have at least 95% sequence identity to specified exemplary sequences set forth in the sequence listing, and claims 31 and 33 require that the sequences share at least 90% sequence identity. As discussed above regarding such claim limitations, Applicants believe that the recitation of a high percentage of sequence identity is a very predictable structure of the primary nucleotide sequences encompassed by the claimed invention.

In summary, the description of a representative number of species *does not* require the description to be of such specificity that it would provide individual support for each species that the genus embraces. The claims in the present application are drawn to specific nucleotide sequences which share a measure of sequence identity with the novel disclosed sequences of the invention. Applicants contend that the present claims and specification meet the 35 U.S.C. §112 written description requirement as clarified by *Eli Lilly* and *Amgen*. See, *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). Applicants have thus provided a structural definition of the sequences of the invention by providing the exemplary nucleotide sequences set forth in SEQ ID NOs: 2, 4, 7, and 10. Applicants have also provided assays by which those of skill in the art can readily assess whether

a nucleic acid molecule meeting the nucleotide sequence element of the claims also meets the functional limitation element of the claims. This is what *Eli Lilly* requires. Thus, Applicants have also conceived the sequences of the invention as articulated in *Amgen*; that is, Applicants are able "to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it." *Amgen*, 927 F.2d 1200, 1206, 18 USPQ2d at 1021.

Applicants submit that the relevant identifying physical and chemical properties of the disclosed genus would be clearly recognized by one of skill in the art and that therefore, Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genus. Accordingly, the rejection of claims 1-33 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn and not applied to the claims as amended.

Consideration Of Previously Submitted Information Disclosure Statement

It is noted that initialed copies of the PTO Forms 1449 that were submitted with Applicants' Information Disclosure Statement filed June 15, 2001 and December 11, 2002 have not been returned to Applicants' representative. Accordingly, it is requested that an initialed copy of these Forms 1449 be forwarded to the undersigned with the next communication from the PTO. In order to facilitate review of the references by the Examiner, copies of the Information Disclosure Statement and the Forms 1449 are attached hereto. Applicants note that this is the third time that the IDS of June 15, 2001 has been included in mailings to the PTO. Copies of the cited references were provided at the time of filling the original Information Disclosure Statement, and, therefore, no additional copies of the references are submitted herewith. Applicants will be pleased to provide additional copies of the references upon the Examiner's request if it proves difficult to locate the original references.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that the rejections of the claims under 35 U.S.C. §§112, first and second paragraphs, are overcome. Applicants

respectfully submit that this application is now in condition for allowance. Early notice to this effect is solicited.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject Application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those, which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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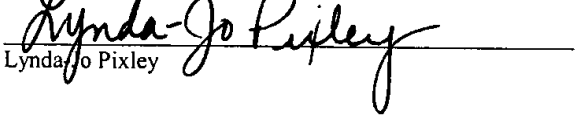

Lynda Jo Pixley